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A Predictive Model for Selecting the Optimal Dose of Carbimazole in Graves' Disease

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INTRODUCTION

The three main modalities of treatment for Graves' disease are anti-thyroid drugs (ATD), radiation therapy and surgery. Anti-thyroid drugs remain as a popular first-line therapy in most parts of Asia and Europe.

Carbimazole is the most frequently used drug in our practice for Graves' disease. Despite over 70 years of use, we can still debate the optimal starting dose of ATD. Some patients respond rapidly to very low doses while others who receive very high doses fail to respond.

In this study, our primary objective is to identify the clinical and/or biochemical factors that affect time to euthyroidism following the initiation of Carbimazole in Graves' disease.

MATERIAL AND METHODS

Medical records of all patients treated at the outpatient endocrine/surgical clinic at 2 tertiary referral hospitals (UKM & Klang Hospital) were reviewed. 190 patients fit the inclusion & exclusion criteria, but 5 were withdrawn due to side effects from Carbimazole. 185 patient records were analyzed, data was collected at baseline and during clinic follow up; subsequently statistical analysis performed. A prediction model was then generated.

RESULTS

Multiple regression analysis was used as a statistical analysis tool. Our study was able to determine that T4 level and weight have a direct relationship with the Carbimazole dose required to achieve euthyroidism. Higher doses are required as the T4 level and weight increases.

We can also conclude that when given the optimal dose, the patient will achieve euthyroidism within 4 to 6 weeks. There are slight differences with regards to age, with the elderly responding faster, however the difference is small, and measures only in days.

A dose prediction model in the form of an easy reference table was generated.

DISCUSSION AND CONCLUSION

Our study has determined that T4 level and weight have a direct relationship with the Carbimazole dose required to achieve euthyroidism. By combining the above 2 variables, we were able to generate a prediction table for the optimal starting dose, ranging from 12mg to 30mg. When given the optimal dose, the patient will achieve euthyroidism within 4 to 6 weeks

Prescription of the optimum lowest dose of Carbimazole in Graves' disease based on T4 levels and patient weight will minimize the potential of drug adverse effects, while eliminating the disease state in the shortest amount of time, and avoiding episodes of hypothyroidism. Future studies should use our prediction model to treat patients and to validate this tool in clinical practice.

Table 1 : Optimal dose range based on fitted regression model

T4 VALUE	WEIGHT									
	30	35	40	45	50	55	60	65	70	75
20	12.245	13.07	13.895	14.72	15.545	16.37	17.195	18.02	18.845	19.67
30	12.865	13.175	13.485	13.795	14.105	14.415	14.725	15.035	15.345	15.655
40	14.515	14.825	15.135	15.445	15.755	16.065	16.375	16.685	16.995	17.305
50	16.165	16.475	16.785	17.095	17.405	17.715	18.025	18.335	18.645	18.955
60	17.815	18.125	18.435	18.745	19.055	19.365	19.675	19.985	20.295	20.605
70	19.465	19.775	20.085	20.395	20.705	21.015	21.325	21.635	21.945	22.255
80	21.115	21.425	21.735	22.045	22.355	22.665	22.975	23.285	23.595	23.905
90	22.765	23.075	23.385	23.695	24.005	24.315	24.625	24.935	25.245	25.555
100	24.415	24.725	25.035	25.345	25.655	25.965	26.275	26.585	26.895	27.205
110	26.065	26.375	26.685	26.995	27.305	27.615	27.925	28.235	28.545	28.855
120	27.715	28.025	28.335	28.645	28.955	29.265	29.575	29.885	30.195	30.505

Table 2 : Weeks taken to reach euthyroidism

T4 VALUE	AGE									
	20	25	30	35	40	45	50	55	60	65	70
20	4.821	4.809	4.797	4.785	4.773	4.760	4.748	4.735	4.722	4.709	4.696
30	5.240	5.232	5.224	5.216	5.208	5.200	5.192	5.184	5.176	5.167	5.159
40	5.534	5.528	5.522	5.516	5.510	5.504	5.499	5.493	5.486	5.480	5.474
50	5.761	5.756	5.752	5.747	5.742	5.738	5.733	5.728	5.723	5.719	5.714
60	5.946	5.942	5.938	5.934	5.930	5.926	5.923	5.919	5.915	5.911	5.907
70	6.102	6.098	6.095	6.092	6.089	6.085	6.082	6.079	6.075	6.072	6.068
80	6.237	6.234	6.231	6.228	6.225	6.222	6.219	6.216	6.214	6.211	6.208
90	6.356	6.353	6.350	6.348	6.345	6.343	6.340	6.338	6.335	6.332	6.330
100	6.462	6.459	6.457	6.455	6.453	6.450	6.448	6.446	6.443	6.441	6.439
110	6.558	6.556	6.554	6.552	6.549	6.547	6.545	6.543	6.541	6.539	6.537
120	6.645	6.643	6.642	6.640	6.638	6.636	6.634	6.632	6.630	6.628	6.626